

Applicants : Stan Gronthos and Andrew Zannettino  
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**REMARKS**

Claims 172, 175-181, 183-186, and 191-194 are currently pending in the subject application. Applicants have hereinabove cancelled claim 183 without prejudice or disclaimer to applicants' right to pursue the subject matter of the claim in the future. Applicants have hereinabove amended claims 172, 176, and 192. Applicants have also added new claims 195 and 196.

Support for amended claim 172 can be found *inter alia* in the specification as filed at page 4, lines 19-23, page 4, line 31 to page 5, line 3, and page 16, lines 13-16.

Support for amended claims 176 can be found *inter alia* in the specification as filed at page 18, line 30 and page 19, line 8 and lines 19-21.

Support for amended claim 192 can be found *inter alia* in the specification as filed at page 18, lines 10-17.

Support for new claims 195 and 196 can be found *inter alia* in the specification as filed at page 12, lines 19-21.

Accordingly, applicants submit that amended claims 172, 176, and 192 and new claims 195 and 196 introduce no new subject matter and are fully supported by the application as originally filed. Upon entry of this Amendment, claims 172, 175-181, 184-186, 191-196 will be pending and under examination.

**Withdrawn Objections**

Applicants note that in the January 19, 2011 Office Action the Examiner has withdrawn the rejection of claims 172, 175-181, 183-186 and 191-194 under 35 U.S.C. § 103(c) over Chopp et al. in view of Jones et al, Bianco et al., and Dennis et al. The

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Examiner has also withdrawn the rejection of claims 172, 175-181, 183-186 and 191-194 under 35 U.S.C. §112, first paragraph.

**Rejection Under 35 U.S.C. §112, Second Paragraph - Indefiniteness**

In the January 19, 2011 Office Action, the Examiner rejected claims 172, 175, 176, 180, 181, 183, 192, and dependent claims under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly pointing out and distinctly claiming the subject matter which the applicants regard as the invention.

**Claim 172**

The Examiner asserted the phrase "a population of cells enriched for MPCs that express the marker STRO-1 or cultured or expanded cells derived therefrom" makes the claim omnibus. The Examiner also asserted that it is unclear whether the MPCs, or the MPCs expressing the marker STRO-1, are cultured or expanded.

**Applicants' Response**

In response, applicants respectfully traverse this rejection. However, without conceding the correctness of the Examiner's argument, applicants have amended claim 172 hereinabove to recite a method ". . . comprising contacting the first tissue with a population of cells enriched for mesenchymal precursor cells (MPCs) that express the marker STRO-1 or progeny of the MPCs that express the marker STRO-1, so as to thereby generate new blood vessels or to repair existing blood vessels in the first tissue." (Emphasis added)

The subject application demonstrates that the claimed population of cells can be enriched for progeny of MPCs that express the marker STRO-1, as indicated on, for example, page 22, lines 24-28; page 31, lines 7-10; and Figure 17. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this rejection.

**Claims 175 and 176**

The Examiner asserted that claims 175 and 176 are indefinite because the phrase "0.01% MPCs capable of forming clonogenic colony" implies that the base claim, i.e. claim 172, encompasses compositions in which MPCs are incapable of forming clonogenic colonies.

**Applicants' Response**

In response, applicants respectfully traverse the Examiner's rejection. Each of claims 175 and 176 depends from claim 172 and further specifies the population of cells comprising a minimal level of the MPCs capable of forming a clonogenic colony. In particular, claim 175 requires that "the population of cells comprises at least 0.01% MPCs capable of forming a clonogenic colony". Claim 176 requires that "the population of cells comprises at least 0.1% MPCs capable of forming a clonogenic colony". Claim 172 thus encompasses a population of cells comprising MPCs capable of forming a clonogenic colony, without specifying a minimal level of such MPCs.

Moreover, while claims 175 and 176 further define the MPC feature of claim 172 by reciting the specified levels of the MPCs in the population of cells, these dependent claims do not define the progeny of the MPCs recited in claim 172. Thus, claim 172 encompasses a population of cells enriched for MPCs capable of forming a clonogenic colony or the progeny of such MPCs, whereas claims 175 and 176 require at least a minimal percentage of the MPCs capable of forming a clonogenic colony.

Accordingly, applicants respectfully submit that claims 175 and 176 are not indefinite. Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

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**Claims 180, 181, 183, and 192**

The Examiner asserted that claims 180, 181, 183, and 192 are indefinite because the claims' recitation of cells expressing "one or more markers", "additional markers", "but not limited to", etc, imply that the parent claim is "presenting the markers in broader context". The Examiner also asserted that applicants have not described the broader genera of cells without said markers.

**Applicants' Response**

In response, applicants respectfully traverse the Examiner's rejection. Without conceding the correctness of the Examiner's argument, applicants have hereinabove cancelled claim 183 without prejudice or disclaimer to applicants' right to pursue the subject matter of the claim in the future.

With respect to claims 180, 181 and 192, applicants note that the specification of the subject application discloses various sub-populations of STRO-1 expressing MPCs that also express additional cell surface markers. For example, the specification discloses on page 29 that about 82% of colony forming cells from dental pulp express STRO-1, whereas 95% express CD146 and 14% express 3G5. Figures 9-11 also show that there are sub-populations of STRO-1 expressing MPCs that express additional markers, in this case CD146 or 3G5.

Applicants have previously demonstrated in the Amendment filed March 29, 2010 in connection with the subject application that the specification discloses the use of STRO-1 expressing MPCs in the manner claimed. Applicants demonstrate above that the specification also discloses subsets of STRO-1 expressing MPCs that also express some, but not necessarily all, of the recited markers. Applicants respectfully submit that claims 180, 181, and 192 define these sub-populations of STRO-1 expressing MPCs. Accordingly, applicants respectfully request that the Examiner

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reconsider and withdraw this ground of rejection.

**Claim Rejections Under 35 U.S.C. §102 - Anticipation**

**Al-Khalidi et al.**

The Examiner rejected claims 172, 175, 176, 184, and 193 under 35 U.S.C. §102(a) as being anticipated by Al-Khalidi et al. (2003, Ann, Thoracic. Surg. 75:204-209). The Examiner asserted that Al-Khalidi et al. teach "a method of promoting or inducing angiogenesis using autologous marrow stromal cells (mesenchymal precursor cells) in a hind limb ischemia of a rat". The Examiner also asserted that Al-Khalidi et al. "conclude that MSC or/MPCs [sic] could be used as therapy to promote angiogenesis as further evidenced by his demonstration using the rat model (p. 208-209)". The Examiner further asserted that "[u]nless reasons to believe other wise Al-Khalidi's MPCs did express STRO-1 and other markers of MPCs claimed."

**Applicants' Response**

In response, applicants respectfully traverse the Examiner's rejection. Al-Khalidi et al. do not mention mesenchymal progenitor cells (MPCs) at all. Instead, Al-Khalidi et al. discuss marrow stromal cells (MSCs). In rejecting the pending claims the Examiner equates MSCs with MPCs, but did not provide any evidence for doing so.

Applicants respectfully submit that MPCs express the marker STRO-1, as recited in the pending claims, are not co-extensive with MSCs of Al-Khalidi et al. Al-Khalidi et al. describe that cells were isolated by adherence to cell culture dishes (page 204, right column). Applicants respectfully direct the Examiner's attention to U.S. Patent No. 6,087,113 ("the '113 Patent"), which describes immuno-phenotypic profiling of MSCs isolated by adherence to cell culture plasticware. Table 5 of the '113

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Patent discloses that MSCs isolated by adherence to cell culture plasticware do not express STRO-1 marker. This is consistent with Table 1 of the subject application, which demonstrates that MSCs are STRO-1 negative, whereas MPCs are STRO-1 positive. Therefore, the cells disclosed in Al-Khalidi et al. do not express STRO-1 marker and differ from the population of cells recited in the pending claims.

Applicants note that the Examiner's rejection is based on inherent anticipation as the Examiner has not shown the cells disclosed in Al-Khalidi et al. actually express STRO-1 marker. However, the Examiner's assumption that the cells disclosed in Al-Khalidi et al. may express STRO-1 marker is not a sufficient basis for an allegation of anticipation based on an inherent disclosure. Applicants respectfully direct the Examiner's attention to M.P.E.P. §2112 (referring to *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed Cir. 1993)) which notes that the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. Rather, "[t]o establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference... Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'" (Emphasis added) See M.P.E.P. §2112 (quoting *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted)).

Accordingly, since Al-Khalidi et al. do not teach a population of cells enriched for MPCs that express the marker STRO-1 as recited in the pending claims, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

**Dennis et al.**

The Examiner rejected claims 172, 175, 176, 184, 191, and 193 under 35 U.S.C. §102(a) as being anticipated by Dennis et al. (2002, Cells Tissues Organs, 170:73-82). The Examiner asserted that Dennis et al. teach a "method of repairing vascular tissue with hematopoiesis [sic] supportive stromal cells with a vascular smooth muscle-like phenotype and bearing Stro-1 marker". The Examiner also asserted that Dennis et al. teach "that human bone marrow derived STRO-1+ cells differentiate into multiple phenotypes including vascular smooth muscle cells". The Examiner further asserted that Dennis et al. teach "using the above cells for the repair of various mesenchymal tissues" and that "[u]nless reasons to believe otherwise these cells induce vascular tissues in the tissues repaired".

**Applicants' Response**

In response, applicants respectfully traverse the rejection. Dennis et al. describe a study testing whether a population of bone marrow-derived STRO-1+ cells can support hematopoiesis. Dennis et al. also disclose that the STRO-1+ cells that support hematopoiesis share some ultrastructural similarities with cells that occur in atheroma plaque of human aorta, i.e. foam cells. However, there is no evidence indicating that the cells disclosed could induce formation or repair of blood vessels. There is also no evidence indicating that these cells are MPCs.

Applicants note that the Examiner's rejection is based on inherent anticipation as the Examiner has not shown the cells disclosed in Dennis et al. "induce vascular tissues in the tissues to be repaired." In fact, Dennis et al. do not teach that STRO-1+ cells from bone marrow (whether MPC or otherwise) differentiate into vascular smooth muscle cells. This reference merely suggests the cells studied therein share some ultrastructural features with foam cells, which can be derived from a macrophage or vascular smooth muscle cell, and also shares

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some ultrastructural features with adipocytes (e.g., polarization and the presence of lipid-laden vesicles). This is far from demonstrating MPCs expressing STRO-1 marker differentiate into vascular smooth muscle cells. As discussed above in connection with Al-Khalidi et al., a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic.

Moreover, since Dennis et al. do not concern studying of vascularization, the reference does not demonstrate "repairing vascular tissue". Dennis et al. show the ability of bone marrow-derived cells to support hematopoiesis when cultured in the presence of CD34<sup>+</sup> cells, or the ability of such cells to differentiate into bone, fat or cartilage. There are no data presented showing the cells studied therein induce repairing of vascular tissue, i.e. angiogenesis.

Finally, the pending claims recite contacting a first tissue in need of blood vessel formation or blood vessel repair with the population of cells. Dennis et al. do not mention such tissue, let alone teach contacting such tissue with a population of cells as claimed.

Accordingly, applicants respectfully submit that Dennis et al. do not anticipate the pending claims. Applicants request that the Examiner reconsider and withdraw this rejection.

**Reyes et al.**

The Examiner rejected claims 172, 175, 176, 184, and 193 under 35 U.S.C. §102(a) as being anticipated by Reyes et al. (2002, Clin. Invest., 109:337-346). The Examiner asserts that Reyes et al. teach "therapeutic use for inducing neo-angiogenesis using multipotent adult progenitor cells (MAPC) that co-purifies with mesenchymal stem cell from postnatal human bone marrow." The Examiner also asserted that the MAPCs "are progenitor cells



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(MPCs) for angioblasts that subsequently differentiate into cells that express endothelial markers, and may be important source for cellular angiogenic therapies". The Examiner further stated that "[u]nless reasons to believe other wise Reyes's MSCs or MPCs did express STRO-1 and other markers of MPCs claimed".

#### Applicants' Response

In response, applicants respectfully traverse the rejection. Reyes et al. relate to multipotent adult progenitor cells (MAPCs). Reyes et al. do not mention MPCs or whether the disclosed cells express STRO-1 marker. In fact, Reyes et al. disclose that MAPC cells were isolated by adherence to cell culture dishes (paragraph bridging pages 337-338). As discussed above in connection with Al-Khaldi et al., knowledge in the art and disclosure of the subject application indicate that such cells do not express STRO-1 marker.

In this regards, applicants respectfully direct the Examiner's attention PCT International Publication No. WO 2001/011011, a copy of which is attached hereto as **Exhibit 1**, on which Reyes is named as an inventor. WO 2001/011011 discloses a method for preparing MAPC cells which appears to correspond to the method described in Reyes et al. (2001, Blood 98:2615-2625, "Reyes II", a copy of which is attached hereto as **Exhibit 2**). The same method was also used to isolate MAPCs in the cited reference, Reyes et al. WO 2001/011011 explicitly states on page 25, lines 21-25, that MAPCs do not express STRO-1. This observation is consistent with the disclosure at paragraph [0067] of U.S. Patent Application Publication No. 2008/0274088.

Applicants further note that the Examiner's rejection is based on inherent anticipation as the Examiner has not shown the cells disclosed in Reyes et al. actually express the STRO-1 marker. As discussed above in connection with Al-Khaldi et al., a certain

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result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic.

Accordingly, applicants respectfully submit that Reyes et al. do not anticipate the claimed invention. Applicants request that the Examiner reconsider and withdraw this rejection.

**Simmons et al.**

The Examiner rejected claims 172, 175, 176, 184, 191, 193, and 194 under 35 U.S.C. §102(a) as being anticipated by Simmons et al. (WO 01/04268 A1). The Examiner asserted that Simmons et al. teach "MPCs with all the claims markers of the instant invention and further claims the use of these MPCs for cell therapies of various tissues".

**Applicants' Response**

Applicants respectfully traverse the rejection. Simmon et al. teach a method of enriching mesenchymal precursor cells. Simmon et al. disclose that the enriched MPCs may be used to repair articular cartilage, repair bone, anchor prosthetic devices, in gene therapy, or in marrow transplantation. The pending claims recite "[a] method of inducing formation or repair of blood vessels in a first tissue in need of blood vessel formation or blood vessel repair, comprising contacting the first tissue with a population of cells enriched for mesenchymal precursor cells . . . ." Simmons et al. do not disclose contacting such a tissue with the enriched MPCs, thus do not anticipate the pending claims. Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

**Kocher et al.**

The Examiner rejected claims 172, 175, 176, 184, 191, 193, and 194 under 35 U.S.C. §102(a) as being anticipated by Kocher et al.

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(2001, Nature Medicine, 7:430-436). The Examiner asserted that Kocher et al. teach "a method of inducing angiogenesis or neovascularization of ischemic myocardium by human bone marrow derived angioblasts (MPCs) that act as endothelial precursors and improves cardiac function". The Examiner also asserted that "[u]nless reasons to believe other wise Kochers MPCs did express Stro-1 and other markers of MPCs claimed".

#### Applicants' Response

In response, applicants respectfully traverse this rejection. Applicants note that the Examiner's rejection is based on inherent anticipation as the Examiner has not shown the cells disclosed in Kocher et al. actually express the STRO-1 marker.

Kocher et al. only disclose that cells were isolated "using a monoclonal antibody against CD34" (Page 430, right column, last paragraph) and the CD34<sup>+</sup> cells were used in the subsequent experiments. However, Example 2 of the subject application discloses that "adult human bone marrow MPC are distinct from stromal precursor cells, haematopoietic stem cells and angioblasts by their high expression of the STRO-1 antigen and lack of CD34 expression". Accordingly, the subject application shows that MPCs express the STRO-1 marker but do not express CD34. This also shows that the cells described in Kocher et al. are not necessarily the same as population of cells recited in the pending claims.

As discussed above in connection with Al-Khalidi et al., a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

#### Chopp et al.

The Examiner rejected claims 172, 175, 176, 184, and 193 under 35

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U.S.C. §102(a) as being anticipated by Chopp et al. (2002, Lancet Neurology, 1:92-100). The Examiner asserted that Chopp et al. teach "a method of promoting angiogenesis during a treatment of neural injury with bone marrow stromal cell including mesenchymal stem cells (MSC) following in vivo and systemic administration of said cell in rats". The Examiner also asserted that Chopp et al. teach "direct implantation, injection as well as systemic administration of said cells including intravenous delivery and effect the recovery from pathological process by regenerative angiogenesis, vasculogenesis". The Examiner further asserted that "[u]nless reasons to believe other wise Chopp's MSCs or MPCs did express Stro-1 and other markers of MPCs claimed."

#### Applicants' Response

Applicants respectfully traverse the Examiner's rejection. Applicants note that the Examiner's rejection is based on inherent anticipation as the Examiner has not shown the cells disclosed in Chopp et al. actually express the STRO-1 marker. As applicants demonstrated in the Amendment filed March 29, 2010 in connection with the subject application and reiterated hereinbelow, the Examiner has incorrectly concluded that the cells described in Chopp et al. inherently express STRO-1.

The Examiner acknowledged at page 8 of the January 19, 2011 Office Action that the teachings in Chopp et al. relate to mesenchymal stem cells (MSCs). This is also evident throughout the cited reference. For example, Chopp et al. stated in the Abstract that the cells are "MSC; an uncharacterized mixed population of plastic adherent cells". Figures 2 and 3 also explicitly refer to the cells as MSCs. As discussed above in connection with Al-Khalidi et al., Table 1 (page 44) of the subject application shows that one distinction between MPCs and MSCs is that MSCs do not express STRO-1. Chopp et al. do not provide contrary evidence regarding MSC cell surface markers. Chopp et al. thus cannot necessarily and inevitably teach

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administration of a population of cell enriched for MPCs that express the marker STRO-1 to induce blood vessel formation and/or repair, as is required in an anticipation rejection based on inherency.

Moreover, Chopp et al. is a review article that merely sets out the *theories* of the authors and reviews literatures that the authors consider to support those theories. For example, at page 96, right column, authors clearly state that the "*operational hypothesis* is that therapeutic benefit [of MSCs] is induced by a series of events..." (Emphasis added).

Accordingly, the Examiner's assumption that the cells disclosed in Chopp et al. may express STRO-1 is not a sufficient basis for an allegation of inherent anticipation. Since Chopp et al. do not teach a population of cells enriched for MPCs that express the marker STRO-1 as recited in the pending claims, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

#### **Claim Rejection Under 35 U.S.C. §103 - Obviousness**

The Examiner asserted that claims 172, 175-181, 183-186, and 191-194 were obvious under 35 U.S.C. §103(c) over the combined teachings of Reyes et al., in view of Jones et al. (2002, *Arthritis and Rheumatism*, 46:3349-3360), Bianco et al. (2001, *Stem Cells*, 19:180-192), Dennis et al., Simmons et al., and Kocher et al.

The Examiner asserted it would have been obvious for a skilled artisan to combine "the method of promoting angiogenesis in an organ or tissue by administering MAPCs (MPCs) as taught by Reyes" with a step of "confirming the identity of MSCs and MPCs as Strol+ or Strol+bright and enriching them as taught by Jones, Simmons, Dennis and/or Bianco" to administer an effective amount

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of cells enriched for MPCs expressing STRO-1 to induce neovascularization in a tissue or myocardium as "Kocher and Dennis teaches that they can differentiate into vascular smooth muscle cell and endothelial cell phenotype and induce vascularization." The Examiner also asserted that the newly cited prior art references teach that "CFU-F fraction of BM cells clearly are enriched in cell comprising Stro1+ cells" and that "these cells are capable of inducing vascularization in vivo and/or progenitors of vascular tissue cells that are capable [of] repairing vascular tissue and myocardium." The Examiner further asserted that Jones et al. and Simmons et al. teach "enrichment of STRO1+ cells in BM derived MPCs."

#### Applicants' Response

In response, applicants respectfully traverse this rejection.

Applicants have shown above that Reyes et al. disclose MAPCs, which do not express the STRO-1 marker. Therefore, if skilled artisans were to "[confirm] the identity of MSCs and MPCs", as suggested by the Examiner, they would have confirmed what was already known in the art, i.e., MAPCs do not express STRO-1. Based on this information the skilled artisan would understand Reyes et al. to teach inducing angiogenesis using cells which do not express the STRO-1 marker.

Moreover, none of the other cited references suggests using MPCs that express STRO-1 marker to induce formation or repair of blood vessels. Applicants have shown above that the cells disclosed in Kocher et al. are isolated using antibody against CD34, thus the cells are CD34<sup>+</sup>. The subject application clearly shows that MPCs which express the STRO-1 marker do not express CD34. Therefore, the cells disclosed Kocher et al. are not the same as the MPCs expressing STRO-1 marker recited in the pending claims.

Dennis et al. present no evidence of "repairing vascular tissue

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with hematopoiesis supportive stromal cells" as asserted by the Examiner. As discussed in more detail above, Dennis et al. teach that cells isolated from bone marrow that express STRO-1 can support hematopoiesis and can differentiate into adipose tissue, bone tissue or cartilage tissue. There is no mention of repairing vascular tissue. Nor does this reference suggest contacting "a first tissue in need of blood vessel formation or blood vessel repair" as is required by the claims.

Furthermore, none of the cited references teach cells, in particular MPCs that express the STRO-1 marker, could differentiate into vascular tissue. Bianco et al. show that bone marrow stromal cells are progenitors of skeletal tissue components such as bone, cartilage, the hematopoiesis-supporting stroma and adipocytes (see Abstract). Bianco et al. do not show that bone marrow stromal cells are capable of differentiating into vascular cells. Instead, the reference merely states that the bone marrow stromal cells are potential components of vascular wall. There is no suggestion that the bone marrow stromal cells would be capable of differentiating into vascular cells or inducing blood vessel repair or formation.

The Examiner also asserted that Bianco et al. teach that "isolated stro-1 bright cells exhibit several endothelial markers" at page 185, column 2, second paragraph. Applicants note that the complete sentence actually states that "these cells also exhibit several endothelial markers, although never a true endothelial phenotype". Bianco et al. further state that bone marrow stromal cells express markers of fibroblasts, myofibroblasts and endothelial cells. (Page 182, right column) Accordingly, applicants respectfully submit that mere expression of endothelial markers does not indicate that the cell is an endothelial cell. Thus Bianco et al. do not demonstrate that MPCs that express the STRO-1 marker differentiate into vascular tissue or induce formation pr repair of blood vessels.

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Dennis et al., as discussed above, merely teach that bone marrow stromal cells that express the STRO-1 marker could have a phenotype similar to that of vascular smooth muscle cells "at the ultrastructural level". However, the cells referred to by Dennis are foam cells, which can actually be derived from either smooth muscle cells or macrophages. Furthermore, foam cells do not form blood vessels; they are a cell that has absorbed lipoprotein and are often found within atherosclerotic plaques (as disclosed in Dennis et al. at page 81, right column). A skilled artisan would not be motivated to contact a tissue requiring blood vessel formation or repair with a cell having characteristics of cells associated with serious human blood vessel-related conditions, e.g. atherosclerotic plaques.

Furthermore, Dennis et al. states in the Abstract that ". . . the subset of marrow cells that express the STRO-1 antigen is capable of differentiating into multiple mesenchymal lineages including hematopoiesis-supportive stromal cells with a vascular smooth muscle-like phenotype, adipocytes, osteoblasts and chondrocytes". Dennis et al. fail to present any evidence that the stromal cells of "vascular smooth muscle-like phenotype" could induce formation of blood vessels. The entire reference shows these cells support hematopoiesis, which does not occur in blood vessel formation or repair.

In summary, applicants respectfully submit that the cited references teach toward a different solution to that claimed since a skilled artisan would not be motivated to use STRO-1 expressing MPCs to induce formation or repair of blood vessels in a first tissue in need of blood vessel formation or blood vessel repair based on for the following reasons:



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- Cells that do not express the STRO-1 marker have been shown to induce blood vessel formation (e.g., MSCs of Al-Khalidi et al. or MAPCs of Reyes et al.);
- Cells that express CD34 have been shown to induce blood vessel formation (e.g., angioblasts of Kocher et al.);
- MPCs which express the STRO-1 marker have been shown to differentiate into bone, cartilage, fat, and stroma that supports hematopoiesis (all of which are of the mesenchymal lineage), but not blood vessels (which are of the endothelial lineage); and
- Cited references do not teach or suggest using MPCs which express the STRO-1 marker to induce blood vessel formation or repair.

Accordingly, applicants respectfully maintain that administration of the specific population of cells recited in claim 172 as amended is neither taught or suggested by, nor obvious over, the cited combination of art. Applicants request that the Examiner reconsider and withdraw this rejection.